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IBM Technical Disclosure Bulletins

Term: L1 with production

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## Search History

**DATE: Wednesday, May 21, 2003** Printable Copy Create Case

| Set Name side by side | Query | Hit Count | Set Name result set |
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| *DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ* | | | |
| L6 | L1 with production | 23 | L6 |
| L5 | L1 WITH (production or preparation) | 129 | L5 |
| L4 | L1 same (production or preparation) | 184 | L4 |
| L3 | L1 same (synthe$ or biosynthe$) | 146 | L3 |
| L2 | L1 same (prepar$ or synthe$ or biosynthe$ or method of makin$ or produc$ or manufact$) | 270 | L2 |
| L1 | acarbose | 806 | L1 |

END OF SEARCH HISTORY

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     (FILE 'HOME' ENTERED AT 14:20:28 ON 21 MAY 2003)

     FILE 'BIOSIS, CAPLUS, MEDLINE, EMBASE, SCISEARCH, DRUGU, TOXCENTER,
     PASCAL' ENTERED AT 14:21:02 ON 21 MAY 2003
L1             2 S ACARBOSE AND GLAUCESCENS
L2            70 S ACARBOSE AND STREPTOMYCES
L3            39 DUP REM L2 (31 DUPLICATES REMOVED)
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L3 ANSWER 31 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10

ACCESSION NUMBER: 1993:474003 BIOSIS
DOCUMENT NUMBER: PREV199396107603
TITLE: Alpha-glucosidase inhibitors of microbial origin.
AUTHOR(S): Selezneva, A. A.; Akulov, N. Yu.
CORPORATE SOURCE: All-Union Res. Technol. Inst. Antibiot. Enzymes, Moscow Russia
SOURCE: Biologicheskie Nauki (Moscow), (1992) Vol. 0, No. 2, pp. 25-32.
ISSN: 0470-4606.
DOCUMENT TYPE: Article
LANGUAGE: Russian
SUMMARY LANGUAGE: Russian; English

AB The data on spreading of alpha-glucosidases with microbial origin are given. Physicochemical characteristics of acorbose - a known inhibitor of alpha-glucosidases - and new inhibitor isolated from **Streptomyces** sp. are given in detail.

L3 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:566290 CAPLUS
DOCUMENT NUMBER: 117:166290
TITLE: Rapid assay of glucoamylase using a fluorescence-labeled glucoamylase inhibitor, **acarbose**
AUTHOR(S): Hata, Yoji; Tanaka, Tatsuyuki; Suizu, Tetsuyoshi; Kawato, Akitsugu; Abe, Yasushisa; Imayasu, Satoshi; Ono, Kazuhisa; Oka, Satoru
CORPORATE SOURCE: Res. Inst. Gekkeikan, Gekkeikan Sake Co., Ltd., Kyoto, 612, Japan
SOURCE: Bioscience, Biotechnology, and Biochemistry (1992), 56(8), 1345-6
CODEN: BBBIEJ; ISSN: 0916-8451
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Usually, glucoamylase activity was assayed by measuring the rate of release of glucose from sol. starch. However, in routine anal. the ext. from rice-koji contains a large amt. of glucose and oligosaccharides, and these saccharides affect the assay of the glucoamylase activity. Therefore, the koji-ext. had to be dialyzed before the enzyme assay by the conventional methods. It has been reported however that the pseudooligosaccharides produced by **Streptomyces** castaneglobisporus inhibit fungal glucoamylases, and that affinity columns prepd. with the immobilized glucoamylase inhibitors, the pseudooligosaccharides or **acarbose**, effectively adsorbed glucoamylase from unpasteurized sake. These observations suggested that the substantially high affinity of the inhibitor for glucoamylase ( **acarbose**, Ki = 0.5 .mu.M; maltose, Km = 1.1 mM) might be applicable to the assay of the enzyme. In this study, a rapid assay method for glucoamylases was developed using a fluorescence-labeled glucoamylase inhibitor. **Acarbose** and 2-aminopyridine were chosen as a glucoamylase inhibitor and a fluorescent reagent, resp. 2-Aminopyridine was coupled to **acarbose**. From 1 mg of **acarbose**, 300 .mu.g of purified pyridylaminated (PA-) inhibitor was eluted as a single peak on Shim-pack CLC-ODS (M) (4.6 mm .times. 15 cm, Shimadzu), monitoring the glucoamylase-inhibitory activity and the fluorescent intensity. A protocol for glucoamylase assay using the fluorescence-labeled inhibitor is as follows. A glucoamylase soln. to be assayed was reacted with the PA-inhibitor, and then the glucoamylase-bound PA-inhibitor was removed from the reaction mixt. by an anion-exchange resin. Then, the glucoamylase activity in the sample was represented by the decrement in the fluorescent intensity (Fdec) that was given as the difference between the fluorescent intensity before (Fint) and after (Ffin) the elimination of the fluorescent affinity complex.

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L1 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:6349 BIOSIS
DOCUMENT NUMBER: PREV200200006349
TITLE: Isolation of the biosynthesis genes for pseudo-oligosaccharides from streptomyces **glaucescens** GLA.O, and their use.
AUTHOR(S): Decker, Heinrich (1)
CORPORATE SOURCE: (1) Bremtal Germany
ASSIGNEE: Aventis Pharma Deutschland GmbH, Frankfurt am Main, Germany
PATENT INFORMATION: US 6306627 October 23, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 23, 2001) Vol. 1251, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The invention relates to a recombinant DNA molecule which comprises genes for biosynthesizing **acarbose** and homologous pseudo-oligosaccharides; to oligonucleotide primers for the PCR amplification of the molecule; to proteins which can be obtained by expressing the genes located on a molecule; to vectors and host cells which comprise the above-mentioned DNA molecule; to proteins which are encoded by the DNA molecule; to proteins which are expressed by means of said vectors in said host cells; to processes for preparing **acarbose** by introducing the characterized genes into appropriate host organisms and/or eliminating these genes from the host organisms; to processes for completing the gene cluster of genes for biosynthesizing **acarbose**, to processes for isolating analogous gene clusters in organisms other than Streptomyces **glaucescens** GLA.O, to processes for mutating promoters of endogenous **acarbose** biosynthesis genes for the purpose of increasing the yield of **acarbose**, to the use of Streptomyces **glaucescens** GLA.O for preparing **acarbose** and for preparing mutants of Streptomyces **glaucescens** GLA.O which are optimized with regard to the **acarbose** yield.

L1 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:8333 CAPLUS
DOCUMENT NUMBER: 128:72892
TITLE: Cloning of genes for biosynthesis of **acarbose** and related pseudooligosaccharides from Streptomyces **glaucescens** GLA.O and their uses
INVENTOR(S): Decker, Heinrich
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 19622783 | A1 | 19971211 | DE 1996-19622783 | 19960607 |
| WO 9747748 | A1 | 19971218 | WO 1997-EP2826 | 19970530 |

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| AU 9731701 | A1 | 19980107 | AU 1997-31701 | 19970530 |
| AU 728870 | B2 | 20010118 | | |
| EP 915981 | A1 | 19990519 | EP 1997-927087 | 19970530 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| CN 1223687 | A | 19990721 | CN 1997-195885 | 19970530 |
| BR 9709658 | A | 19990810 | BR 1997-9658 | 19970530 |
| JP 2001507923 | T2 | 20010619 | JP 1998-501137 | 19970530 |
| US 6306627 | B1 | 20011023 | US 1998-194905 | 19980729 |
| KR 2000016470 | A | 20000325 | KR 1998-710054 | 19981205 |
| US 2002192793 | A1 | 20021219 | US 2001-922683 | 20010807 |
| PRIORITY APPLN. INFO.: | | | DE 1996-19622783 A | 19960607 |
| | | | WO 1997-EP2826 W | 19970530 |
| | | | US 1998-194905 A3 | 19980729 |

AB Genes for the enzymes involved in the biosynthesis of the .alpha.-amylase-inhibiting pseudooligosaccharide antibiotics such as **acarbose** are cloned from the producer organism Streptomyces **glaucescens** GLA.O. S. **glaucescens** is genetically well characterized in comparison to the Actinoplanes **acarbose** producers and so may be of greater use in the development of high-producer strains. The gene for dTDP glucose 4,6-dehydratase was cloned by PCR using primers derived from the sequence of previously characterized gene. This gene was used as a probe to obtain a 6.8 kb PstI fragment contg. six genes. The proteins encoded by three of these genes showed similarities to sugar-binding proteins that may be involved in the biosynthesis of **acarbose**.

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INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 13:18:41 ON 21 MAY 2003

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| 21 | FILE CIN |
| 48 | FILE CONFSCI |
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| 589 | FILE DDFU |
| 111 | FILE DGENE |
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| 87 | FILE DRUGMONOG2 |
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| 9 | FILE EMBAL |
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| 135 | FILE PROMT |
| 984 | FILE SCISEARCH |
| 1 | FILE SYNTHLINE |
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| 669 | FILE USPATFULL |
| 52 | FILE USPAT2 |

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               10   FILE VETU
              113   FILE WPIDS
              113   FILE WPINDEX
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L2          1167 S L1 AND (PREPA? OR SYNTHE? OR BIOSYNTHE? OR PRODUCT?)
L3            71 S L2 AND (COLI OR SUBTILIS OR STREPTOMYCES OF NIGER OR CEREVIS
L4            33 DUP REM L3 (38 DUPLICATES REMOVED)

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L4 ANSWER 14 OF 33 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1999:307342 SCISEARCH
THE GENUINE ARTICLE: 186VV
TITLE: The AcbC protein from Actinoplanes species is a C-7-cyclitol synthase related to 3-dehydroquinate synthases and is involved in the **biosynthesis** of the alpha-glucosidase inhibitor **acarbose**
AUTHOR: Stratmann A; Mahmud T; Lee S; Distler J; Floss H G; Piepersberg W (Reprint)
CORPORATE SOURCE: BERG UNIV GESAMTHSCH WUPPERTAL, GAUSS STR 20, D-42097 WUPPERTAL, GERMANY (Reprint); BERG UNIV GESAMTHSCH WUPPERTAL, D-42097 WUPPERTAL, GERMANY; UNIV WASHINGTON, DEPT CHEM, SEATTLE, WA 98195
COUNTRY OF AUTHOR: GERMANY; USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (16 APR 1999) Vol. 274, No. 16, pp. 10889-10896.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 41

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The putative **biosynthetic** gene cluster for the a-glucosidase inhibitor **acarbose** was identified in the producer Actinoplanes sp, 50/110 by cloning a DNA segment containing the conserved gene for dTDP-D-glucose 4,6-dehydratase, acbB. The two flanking genes were acbA (dTDP-D-glucose synthase) and acbC, encoding a protein with significant similarity to 3-dehydroquinate synthases (AroB proteins). The acbC gene was overexpressed heterologously in Streptomyces lividans 66, and the **product** was shown to be a C-7-cyclitol synthase using sedo-heptulose 7-phosphate, but not ido-heptulose 7-phosphate, as its substrate. The cyclization **product**, 2-epi-5-epi-valiolone ((2S,3S,4S,5R)-5-(hydroxymethyl)cyclohexanon-2,3,4,5-tetrol), is a precursor of the valienamine moiety of **acarbose**. A possible five-step reaction mechanism is proposed for the cyclization reaction catalyzed by AcbC based on the recent analysis of the three-dimensional structure of a eukaryotic 3-dehydroquinate synthase domain (Carpenter, E. P., Hawkins, A. R., Frost, J. W., and Brown, K. A. (1998) Nature 394, 299-302).

L4 ANSWER 2 OF 33 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2002:532260 SCISEARCH
THE GENUINE ARTICLE: 564KM
TITLE: **Biosynthesis** of the C-7-cyclitol moiety of **acarbose** in Actinoplanes species SE50/110 - 7-O-phosphorylation of the initial cyclitol precursor leads to proposal of a new **biosynthetic** pathway
AUTHOR: Zhang C S; Stratmann A; Block O; Bruckner R; Podeschwa M; Altenbach H J; Wehmeier U F; Piepersberg W (Reprint)
CORPORATE SOURCE: Berg Univ Gesamthsch Wuppertal, Inst Chem Microbiol, Gauss Str 20, D-42097 Wuppertal, Germany (Reprint); Berg Univ Gesamthsch Wuppertal, Inst Chem Microbiol, D-42097 Wuppertal, Germany; Berg Univ Gesamthsch Wuppertal, Inst Organ Chem, D-42097 Wuppertal, Germany; Res Ctr Julich, Inst Biotechnol 1, D-52425 Julich, Germany
COUNTRY OF AUTHOR: Germany
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (21 JUN 2002) Vol. 277, No. 25, pp. 22853-22862.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3996 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB We have previously demonstrated that the **biosynthesis** of the C-7-cyclitol, called valienol (or valienamine), of the a-glucosidase inhibitor **acarbose** starts from the cyclization of sedo-heptulose 7-phosphate to 2-epi-5-epivaliolone (Stratmann, A., Mahmud, T., Lee, S., Distler, J., Floss, H. G., and Piepersberg, W. (1999) J. Biol. Chem. 274, 10889-10896). **Synthesis** of the intermediate 2-epi-5-epi-valiolone is catalyzed by the cyclase AcbC encoded in the **biosynthetic** (acb) gene cluster of Actinoplanes sp. SE50/110. The acbC gene lies in a possible transcription unit, acbKLMNOC, cluster encompassing putative **biosynthetic** genes for cyclitol conversion. All genes were heterologously expressed in strains of Streptomyces lividans 66 strains 1326, TK23, and TK64. The AcbK protein was identified as the **acarbose** 7-kinase, which had been described earlier (Drepper, A., and Pape, H. (1996) J. Antibiot. (Tokyo) 49, 664-668). The multistep conversion of 2-epi-5-epi-valiolone to the final cyclitol moiety was studied by testing enzymatic mechanisms such as dehydration, reduction, epimerization, and phosphorylation. Thus, a phosphotransferase activity was identified modifying 2-epi-5-epi-valiolone by ATP-dependent phosphorylation. This activity could be attributed to the AcbM protein by verifying this activity in S. lividans strain TK64/pCW4123M, expressing His-tagged AcbM. The His-tagged AcbM protein was purified and subsequently characterized as a 2-epi-5-epi-valiolone 7-kinase, presumably catalyzing the first enzyme reaction in the **biosynthetic** route, leading to an activated form of the intermediate 1-epi-valienol. The AcbK protein could not catalyze the same reaction nor convert any of the other C-7-cyclitol monomers tested. The 2-epi-5-epi-valiolone 7-phosphate was further converted by the AcbO protein to another isomeric and phosphorylated intermediate, which was likely to be the 2-epimer 5-epi-valiolone 7-phosphate. The **products** of both enzyme reactions were characterized by mass spectrometric methods. The **product** of the AcbM-catalyzed reaction, 2-epi-5-epi-valiolone 7-phosphate, was purified on a **preparative** scale and identified by NAIR spectroscopy. A **biosynthetic** pathway for the pseudodisaccharidic acarviosyl moiety of **acarbose** is proposed on the basis of these data.

L4 ANSWER 3 OF 33 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-34942 DRUGU P B

TITLE: **Preparation** and characterization of alpha-D-glucopyranosyl- alpha-acarviosinyl- D-glucopyranose, a novel inhibitor specific for maltose-producing amylase.

AUTHOR: Kim M J; Lee H S; Cho J S; Kim T J; Moon T W; Oh S T; Kim J W; Oh B H; Park K H

CORPORATE SOURCE: Univ.Seoul-Nat.Res.Cent.New-Bio-Mater.; Univ.Chungbuk-Nat.; Univ.Pohang-Sci.Technol.; Univ.Incheon

LOCATION: Suwon, Cheongju, Pohang; Incheon, Korea

SOURCE: Biochemistry (41, No. 29, 9099-108, 2002) 9 Fig. 4 Tab. 36 Ref.

CODEN: BICHAW ISSN: 0006-2960

AVAIL. OF DOC.: Res. Cent. for New Bio-Materials in Agr. + Dept. of Food Science + Technol., School of Agr. Biotechnol., Seoul National University, Suwon 441-744, Korea. (K.H.P.). (e-mail: parkkh@plaza.snu.ac.kr).

LANGUAGE: English

DOCUMENT TYPE: Journal

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

AB Alpha-D-glucopyranosyl- alpha-acarviosinyl- D-glucopyranose (GlcAcvGlc) and **acarbose** showed time-dependent inhibitions against maltogenase (MGase, Novo Nordisk), Thermus maltogenic amylase (ThMA) and cyclomaltodextrinase of alkalophilic Bac. sp. I-5 (CDase I-5, both purified from E. **coli**) in a mixture with p-nitrophenyl-alpha-D-maltoside (PNPG2) as substrate. Inhibition of ThMA and CDase I-5 by **acarbose** or GlcAcvGlc followed mechanism B, while that of MGase followed mechanism A. **Acarbose** more efficiently inhibited maltase and sucrase from the rat intestine. Alpha-amylase from porcine pancreas was more sensitive to GlcAcvGlc than **acarbose**. GlcAcvGlc and **acarbose** did not inhibit sweet potato beta-amylase. GlcAcvGlc increased the dimeric form of ThMA. Therefore, development of **acarbose** derivatives as amylolytic enzyme inhibitors provides a new approach for the management of diabetes.